

TOBACCO INDUSTRY RESEARCH COMMITTEE
150 EAST FORTY SECOND STREET NEW YORK 17, N.Y.

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Application For Research Grant

Date: January 25, 1958

1. Name of Investigator:

Ronald M. Pace

2. Title:

Professor & Chairman, Department of Physiology
and Director, Institute for Cellular Research

3. Institution

University of Nebraska, Lincoln, Nebraska

& Address:

4. Project or Subject:

To study the effects of certain constituents of tobacco
smoke on tissue cells cultivated in vitro.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

We wish to study the effects of certain constituents of tobacco smoke on
several types of tissue cells over short and long periods of time.

We are currently using the following well-established clones of cells:
Earle's strain L fibroblasts, human skin cells, liver cells, and the Hela strain.
It is also our desire to obtain a strain of lung epithelial cells (human) with
the possibility of obtaining a clone.

Studies on the effects of air pollutants on these cell clones have been in
progress during the past 1 1/2 years.

Our specific aims, if the present request is granted, are:

- (1) To study the effects of certain single smoke constituents on the
various strains of cells as well as the effects of various concentra-
tions of oxygen. The effects of mixtures of these smoke constituents
with various concentrations of oxygen will also be observed.
- (2) To culture lung tissue (according to Sax "organ culture" techniques)
in order to study the effects of the smoke constituents on organized
tissue.

The various cell types will be cultivated in as nearly a chemically-defined
medium as possible. In preliminary investigations Earle's medium 109 plus 10%
horse serum has been used.

The first part of these investigations will consist of exposing replicate
cultures of the respective cell clones to various concentrations of a single
constituent of smoke. Both periodic and continuous exposures will be made.

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Special flasks and delivery chambers have been devised so that proper mixtures of these gases can be made and applied to each individual culture.

The second part of the study will be concerned with investigations on the respiratory metabolism of the cells under these different conditions. Perhaps some clues as to the mechanism affected by these substances might be obtained.

The third part of the study will be made in parallel with the first two and will consist of observations on morphological changes that may take place within the cultures or within the cells themselves. This will be accomplished by time-lapse photomicrography so that a permanent record of the effects may be obtained.

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6. Budget Plan:

Salaries	\$7000.00	(\$5500)
Expendable Supplies	750.00	(\$1500)
Permanent Equipment		
Overhead	250.00	
Other (Travel)	6000.00	
Total		

7. Anticipated Duration of Work: 1 year

8. Facilities and Staff Available: A laboratory consisting of a suite of 8 rooms fully equipped for short and long term tissue culture investigation. There are several persons on the staff at present supported by other grants and University funds. These include a Chief Investigator, Co-investigator, Research Associate, Secretary-technician and laboratory helper.

9. Additional Requirements:

10. Additional Information (Including relation of work to other projects and other sources of supply):

Previous and current sources of funds have been awarded by 1) U.S.P.H.S. (grants through National Cancer Institute). 2) U.S.P.H.S. Air Pollution Medical Program (contracts). 3) American Cancer Society. 4) Tobacco Industry Research Committee (Fellowship). 5) Cooper Foundation.

We are at present working on a project designed to give information concerning the effects of air pollutants on Tissue cells cultivated in vitro. This work has actually been in progress for the past 1½ years and at this time we are just about ready to carry out studies on the effects of hydrocarbons and ozonides of same.

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Signature /s./ Donald M. Pace
Director of Project

/s./ Carl A. Donaldson
Business Officer of the Institution